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Clinicopathologic features of incidental prostatic adenocarcinoma in radical cystoprostatectomy specimens

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Abstract

Background: The aim of this study is to review all features of incidentally discovered prostate adenocarcinoma in patients undergoing radical cystoprostatectomy for bladder cancer.

Methods: The medical charts of 300 male patients who underwent radical cystoprostatectomy for bladder cancer between 1997 and 2005 were retrospectively reviewed. The mean age of the patients was 62 (range 51-75) years.

Results: Prostate adenocarcinoma was present in 60 (20%) of 300 specimens. All were acinar adenocarcinoma. Of these, 40 (66.7%) were located in peripheral zone, 20 (33.3%) had pT2a tumor, 12 (20%) had pT2b tumor, 22(36.7%) had pT2c and, 6 (10%) had pT3a tumor. Gleason score was 6 or less in 48 (80%) patients. Surgical margins were negative in 54 (90%) patients, and tumor volume was less than 0.5 cc in 23 (38.3%) patients. Of the 60 incidentally detected cases of prostate adenocarcinoma 40 (66.7%) were considered clinically significant.

Conclusion: Incidentally detected prostate adenocarcinoma is frequently observed in radical cystoprostatectomy specimens. The majority are clinically significant.

Keywords: Bladder cancer, cystoprostatectomy, incidental, prostate cancer

Background

Prostate adenocarcinoma (PCa) is the most common visceral malignancy in the male population and the second leading cause of death in men [1]. It can be found incidentally when the prostate is removed during radical cystoprostatectomy (RCP) for bladder cancer and latently at autopsy or clinically diagnosed by physical examination, laboratory tests, and symptoms [2,3]. In autopsy series incidental prostate cancer is found in 30% of men in their fifth decade and that rate increases to as high as 90% in men aged older than 90 years [4]. The frequency of PCa incidentally discovered in RCP specimens is extremely variable, ranging from 10% to nearly 60% [1,3,5]. These tumors are typically small, well- or moderately well-differentiated, localized entirely within the gland, and most being regarded as clinically insignificant [3,6].

Our aim was to review features of incidentally discovered prostate adenocarcinoma in patients with bladder cancer with regard to their incidence, pathologic characteristics and clinical significance.

Methods

We reviewed the medical charts of 300 men who diagnosed muscle-invasive bladder urothelial carcinoma and no history or clinical evidence of PCa before surgery in 1997-2005. Of these, 60 patients who had concomitant PCa were included in our study. Physical examinations, laboratory studies, chest radiographies and abdominopelvic computed tomography were performed in all patients. The clinical records were obtained at the time of admission, and follow-up information was obtained from hospital records or directly from the patient's families. Patients were evaluated considering to age, tumor focality, tumor location, gleason score, pathological tumor stage, extracapsular extension, seminal vesicle invasion, surgical margin status, tumor volume and clinical significance. The serum prostate-specific

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antigen (PSA) levels were determined routinely before RCP

Histopathological findings were obtained surgically resected specimens from the Department of Pathology files that were evaluated by two pathologists. A routine pathological examination was used for all RCP specimens by sectioning and totally submitting the prostate. The prostate was severed from the bladder and then covered with India ink. After fixation for 24 h in 10% neutral buffered formalin, the prostate specimens were step sectioned at 3 mm intervals perpendicular to the long axis (apical-basal) of the gland. (Between 1997 and 2002, some of the prostate specimens were sliced at an interval of 5 mm). The apex, base and seminal vesicles were removed from each specimen and submitted in total for routine histological examination. The cut specimens examined histological as 2 μm-thick whole-mount haematoxylin and eosin (H&E)-stained sections. The stage of prostate cancer was based on the 2002 revision of the TNM system [7]. The Gleason score was determined using the 2005 International Society of Urological Pathology modified Gleason system [8]. Tumor volume was calculated using the length (L), width (W), and height (number of cross sections × sectional thickness, CST). According to Chen et al. derived the formula = 0.4 (slope of the regression line) × L × W × CST to estimate volume [9].

We defined clinically significant PCa features as any of the following: PCa tumor volume ≥ 0.5 cc, Gleason score ≥ 6, extraprostatic extension, seminal vesicle invasion, and/or a positive surgical margin according to the criterion advocated by Epstein et al. [10]. Data for the present study were identified by a structured MEDLINE search up to 1st September 2010. ''Bladder cancer'', ''cystoprostatectomy'', ''incidental'', and ''prostate cancer'' were the key words for searching the data. Only publications in English were considered. All the studies addressing the incidence, pathological characteristics, and/or clinical significance of prostate tumors were included and reviewed in detail

Results

In this study, a total of 60 patients (20%) were incidentally diagnosed as having PCa in RCP specimens. Detailed characteristics of these 60 are summarized in Table 1. The mean age of the patients was 62 (range 51-75) years. All were acinar adenocarcinoma. Of the 20 adenocarcinoma (33.3%) were pT2a, whereas 12 (20%) and 22(36.6%) were pT2b and pT2c, respectively and 6 adenocarcinoma (10%) was T3a. Of these patients, 32 (53.3%) had clinically significant features. 12 (20%) had Gleason score of > 6, 37(61.7%) had PCa tumor volume ≥ 0.5 cc, 6(10%) had positive surgical margin and 6 (10%) had positive extraprostatic extension. Preoperative PSA was high in 5 patients (ranging between 10-29.05 ng/ml). The characteristics of their PCa were stage T2 in 2 of them and stage T3 in others. Tumor volume was significantly high in these patients. The surgical margin was positive in one of these patients. In 48 specimens (80%), the Gleason score was 6 or less. Negative margins were present in 54 (90%) of cases. Negative

Table 1 The clinicopathological characteristics of incidental prostate cancer at RCP in the 60 patients with bladder cancer

Features	Number of patient's n (%)
Mean age at surgery, years	62
Focality	
Monofocal	46
Multifocal	14
Tumor location	
Peripheral zone	40
Central zone	6
Transition zone	2
All three zones	12
Gleason score	
≤ 6	48
7 (3+4)	6
7 (4+3)	6
8-10	-
pT (TNM system)	
pT2a	20
pT2b	12
pT2c	22
pT3a	6
pT3b	-
pT4	-
Stage of bladder cancer	8
p T1	20
p T2a	26
p T2b	6
p T3a	
Seminal vesicle invasion	
Negative	60
Positive	-
Extraprostatic extension	
Negative	54
Positive	6
Surgical margin status	
Negative	54
Positive	6
Tumor volume, mL	
Range	23
< 0.5	37
≥ 0.5	
Clinically insignificant	20
Clinically significant	40

extraprostatic extension were present in 54 (90%) of cases. None of the patients had seminal vesicle invasion. All cases were pN0 for PCa. In 23 specimens (38.3%), the volume was less than 0.5 cc. Of the 60 cases of incidentally detected prostate cancer, 40 (66.7%) were considered clinically significant. Follow-up data were available for 60 patients. The cause of death was not related to the PCa in any of the patients and there was no PSA recurrence during follow-up of 96 months (range between 72-168 months).

Discussion

RCP represents the most effective treatment for muscle-invasive nonmetastatic bladder cancer [11]. Many authors have reported a higher prevalence of PCa in patients with bladder cancer [12,13], although data are sparse regarding the outcome of these patients [14].

The frequent high coincidence of prostate and bladder cancer occurring together could be explained by a common carcinogenic pathway. In this respect, Singh et al. reported that some tumor suppressor genes such as p53 and Rb play a major role in the development of both prostate and bladder cancers [15]. More recently, Amara et al. demonstrated that prostate stem cell antigen is overexpressed in most human transitional cell carcinomas in an immune-histochemical analysis [16]. However, these represent preliminary experiences and the model for a common carcinogenic pathway remains to be elucidated [1].

According to literature, the proportion of clinically significant cancers in the series published previously varies from 10% to 70% [4-6,12,14,17-33] [Table 2]. This high range between the proportions may be related with hereditary and exogenous factors, such as food consumption and patterns of sexual behavior. The detailed pathological examination of the excised prostatic tissue specimens may be another important factor for the detection of small cancer [31]. In this respect, two important issues are the thickness of the slice of the prostate and whether the prostate is totally embedded [3]. The advantage of complete sampling over partial sampling is that small foci of cancer are seen more frequently. When prostate slices are thicker than 5 mm, small foci of cancer might miss within the slice. By complete sampling, cancer features, such as extraprostatic extrusion and positive margins, are more accurately evaluated [16]. Regarding the published reports in Table 2, Mazzucchelli et al [3] found a 49.6% rate of incidental

Table 2 PCa in cystoprostatectomy specimens: literature overview.

References	Year	No.of Patients	Mean age (year)	Slice Thickness (mm)	Sampling of prostate	No. of prostate cancer (%)	No. of significant prostate cancer (%)
Abbas [17]	1996	40	64.3	2-3	Partial	18(45)	6(33)
Moutzouris [18]	1999	59	66.5	5	Complete	16 (27)	NA
Aydin [19]	1999	121	67.1	NA	NA	17 (14.0)	NA
Yang [20]	1999	49	67	8 3	Complete	16 (33)	NA
Conrad [21]	2001	133	60	3	Complete	58 (43.6)	11 (19)
Prange [22]	2001	85	64	4	Complete	41(48)	4(10)
Cindolo [23]	2001	165	69	3	Partial/complete	17(10.3)	NA
Ward [24]	2004	129	69	NA	NA	30(23.3)	18(60)
Revelo [25]	2004	121	67.4	5	Complete	50(41.3)	24(48)
Kouriefs [26]	2005	128	NA	NA	NA	23(18.0)	NA
Delongchamps [14]	2005	141	62	4	Complete	20(14.2)	14(70)
Ruffion [12]	2005	100	62	2.5	Complete	51 (51.0)	6 (12)
Lee [6]	2006	248	63.5	NA	Complete	10 (4.0)	NA
Rocco [27]	2006	63	67	3	Complete	34 (54)	12 (35)
Abdelhady [5]	2007	204	67	NA	Complete	58 (28.4)	18 (31)
Winkler [32]	2007	97	NA	2	Partial	58 (60)	31 (53)
Hosseini [28]	2007	50	62.5	NA	Partial	7 (14)	4 (57)
Weizer [29]	2007	35	65	NA	NA	16 (46)	4 (25)
Jin [31]	2008	264	70.9	5	Complete	37 (14)	12 (32.4)
Mazzucchelli [4]	2009	248	68	3	Complete	123 (49.6)	23 (18.7)
Nakagawa [33]	2009	349	65	5	NA	91 (26.1)	68 (74.7)
Gakis [30]	2010	95	68	4-5	NA	26 (27)	7 (27)
Present study	*2010*	*300*	*62*	*3-5*	*Complete*	*60(20)*	*40(66.6)*

PCa, in RCP specimens with serial step slices taken at 2-3-mm intervals. However, the incidence was lower in studies using a different pathological examination protocol. For instance, Jin et al. identified PCa in 14% of the examined specimens when using 5-mm thick slices [31].

In our study between 1997 and 2002 the prostate specimens were sliced at an interval of 5 mm. At the same interval 160 patients were underwent RCP and only 14 patients (8.75%) with incidental PCa were identified. Probably several incidental cancers might have been missed in this interval. After 2002 prostate specimens were evaluated with slices taken every 3 mm from the base to the apex of the gland, as is usually done for RCP, there was incidental PCa in 46 of 140 patients (32.8%) who underwent RCP. We believe that using slices taken every 2-3 mm, could detect a higher incidence of PCa.

Stamey et al. first defined the clinically significant adenocarcinoma of PCa in RCP specimens [34]. According to these autours clinically significant prostate cancer is based on Gleason score, tumour volume and stage, lymph node status and resection margin [34]. After than Epstein et al. defined clinically insignificant PCa features: (1) a Gleason score ≤ 6 without Gleason pattern 4 or 5, (2) organ-confined disease (no extraprostatic extension, seminal vesicle invasion, or lymph node involvement and (3) a tumour volume < 0.5 cm3 [10]. We evaluated clinically significant PCa features as any of the following: PCa tumor volume > 0.5 cc, Gleason score > 6, extracapsular extension, seminal vesicle invasion, and/or a positive surgical margin according to the criterion advocated by Epstein et al. According to this definition, the ratio of clinically significant PCa in our study was 66.7% (40/60) and this is a remarkable ratio.

Careful preoperative evaluation to diagnose concurrent PCa is very important [30]. Some authors have tried to use PSA into predictive models of tumor significance. Stamey et al. reported that serum PSA had been associated with cancer volume [34]. Winkler investigated the relationship between PSA level and tumour volume for incidental adenocarcinoma of the prostate found in RCP specimens. According to this study, the median PSA level for patients with and without prostate cancer was not significantly different [32]. The correlation between tumor volume and PSA level is also controversial [32]. Although in our series, tumor volume was high in patients with elevated levels of PSA, the number of these patients is not enough to advocate this relationship. In patients with PSA > 4 ng/mL or a palpable nodule a meticulous dissection of prostate during RCP should be performed.

According to Delongchamps et al. the outcome of patients with incidental prostate ca after RCP depends on the prognosis of bladder tumor [14]. In their report on 141 patients, twenty of them had incidental PCa and no patient experienced PSA recurrence during the follow-up. [14]. Pritchett et al. reported no worse survival in patients with both cancers compared with those with bladder cancer alone [35]. Wolters et al demonstrated that screen detected prostate cancer treated with radical prostatectomy shows more aggressive features than incidentally found prostate cancer [36]. In our study, PSA did not reach the nadir < 0.2 ng/mL (considered the cut-off value of biochemical recurrence for PCa) in a mean follow-up of 96 months (range, 72-168 months). All of the patients with incidental PCa were still alive. These findings show that incidental PCa does not influence prognosis and suggest that the outcome of patients with incidentally discovered PCa after RCP depends on the prognosis of the bladder cancer.

Conclusions

The reported incidence of PCa in RCP specimens is highly variable and mostly depending on the histopathology technique of sampling. PSA cannot identify asymptomatic PCa, so there is still no effective tool for the detection of PCa before surgery. In line with published reports, incidental PCa does not impact the prognosis of bladder cancer patients undergoing RCP. The clinical significance of these incidentally discovered cancers remains questionable, as the outcome of patients depends on the prognosis of the bladder tumor.

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Authors' contributions

BA and HV both participated equally in literature search, conceptualization and preparation of the manuscript. Both authors have read the manuscript and approve it for publication.

Competing interests

The authors declare that they have no competing interests.

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